STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 175655

TO: Andrew D Kosar **Location: 3c04 / 3c18** **Art Unit: 1654** **Friday, January 13, 2006** **Case Serial Number: 10/798218**	**From: Noble Jarrell** **Location: Biotech-Chem Library** **Rem 1B71** **Phone: 272-2556** **Noble.jarrell@uspto.gov**

Search Notes

Access DB# 175655

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: **Andrew D. Kosar** Examiner# : **80341** Date: **1/4/06**

Art Unit: **1654** Phone Number: **(571)272-0913** Serial Number: 10/798,218

Mail Box and Bldg/Room Location: **Mail: REM 3c18** Results Format Preferred (circle): **Paper** Disk E-mail
Office: REM 3c04

MEI

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Organic compounds with biological activity as thrombin inhibitors and use thereof

Inventors (please provide full names): Marcel Thurk

Earliest Priority Filing Date: 9/10/2002 (US PCT); 9/10/2001 (Germany)

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Please search the following peptide compound, corresponding to attached claim 177. The claim is drawn to hexapeptides with terminal modification(s).

(each position can be L or D)

X1 is Val, Ala, Leu, Ile, Nle, Asn, Gln, Ser, Thr, Tyr, Arg, Lys or Orn

X2 is Val, Ala, Leu, Ile, Nle, Ser, Thr, Tyr, Pro, Cit, Arg, Lys, Orn, His, Glu, Asp, Trp, Cha or Chg

X3 is Cha or Chg

X4 is Pro or Aze

X5 is Tyr or Phe

X6 is Arg, Lys, Orn or Har

X3-X4-X5 make a pseudo tripeptide core structure.

Please note, the compounds may also be des-X1 and/or des-X6

RECEIVED
JAN - 5 2006
CHEMICAL (STIC)

****

STAFF USE ONLY

Searcher: nolle
Searcher Phone:
Searcher Location:
Date Searcher Picked Up: 1/13/06
Date Completed: 1/13/06
Searcher Prep & Review Time: 10
Clerical Prep Time:
Online Time: 49

Type of search

NA Sequence (#)
AA Sequence (#)
Structure (#) 4
Bibliographic ✓
Litigation
Full Text
Patent Family
Other

Vendors and cost where applicable

STN ✓
Dialog
Questel/Orbit
Dr. Link
Lexis/Nexis
Sequence System
WWW/Internet
Other (specify)

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1.-176. Cancelled.

177. (New) A compound of formula (IV)

Y^1-(NH-X^1-C=O)-(NH-X^2-C=O)-(NH-X^3-C=O)-(NH-X^4-C=O)-(NH-X^5-C=O)-(NH-X^6-C=O)-Y^2 (IV),

wherein Y^1 is either

a) a hydrogen or

b) a methyl group or

c) an acetyl group or

d) is characterized by a backbone consisting of a chain of 1 to 32 carbon atoms,

wherein NH-X^1-C=O is a D- or L-amino acid selected from the group consisting of

a) valine ;

b) alanine;

c) leucine;

d) isoleucine;

e) norleucine;

f) asparagine;

g) glutamine;

h) serine;

i) threonine;

j) tyrosine;

k) arginine;

l) lysine; and

m) ornithine,

wherein NH-X^2-C=O is a D- or L-amino acid selected from the group consisting of

a) alanine;

b) valine;

c) leucine;

d) isoleucine;

e) norleucine;

f) serine;

g) threonine;

h) tyrosine;

i) proline;

j) citrulline;

k) arginine;

l) lysine;

m) ornithine;

n) histidine;

o) glutamic acid;

p) aspartic acid;

q) tryptophan;

r) cyclohexylalanine; and

s) cyclohexylglycine,

wherein NH-X^3-C=O is an amino acid selected from the group consisting of

a) L-cyclohexylalanine;

b) D-cyclohexylalanine;

c) L-cyclohexylglycine; and

d) D-cyclohexylglycine,

wherein NH-X^4-C=O is an amino acid selected from the group consisting of

a) L-proline;

b) D-proline;

c) L-azetidine-2-carboxylic acid; and

d) D-azetidine-2-carboxylic acid,

wherein NH-X^5-C=O is an amino acid selected from the group consisting of

a) L-tyrosine;

b) D-tyrosine;

c) L-phenylalanine; and

d) D-phenylalanine,

wherein NH-X^6-C=O is an amino acid selected from the group consisting of

a) L-arginine;

b) D-arginine;

c) L-lysine;

d) D-lysine;

e) L-ornithine;

f) D-ornithine;

g) L-homoarginine; and

h) D-homoarginine,

wherein Y^2 is either

a) an OH group of the C-terminal amino acid having a terminal carboxylic acid group or

b) an amino group where the carboxylic acid group in the C-terminal amino acid is replaced by an amide group or

c) a hydrogen where the carboxylic acid group in the C-terminal amino acid is replaced by an aldehyde group or

d) 7-amido-4-methylcoumarin combined through the carboxylic acid group or

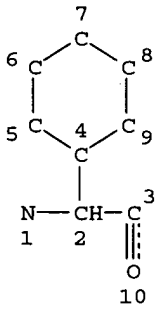
e) para-nitroanilide combined through the carboxylic acid group or

f) is replaced by a connecting chain containing 1 to 35 atoms,

or wherein the compound is a molecule shortened at the C-terminus and/or at the N-terminus by one amino acid, and pharmaceutically acceptable salts thereof.

178. (New) A pharmaceutical composition comprising an effective thrombus-preventing amount of a compound according to claim 177 and a pharmaceutically acceptable carrier.

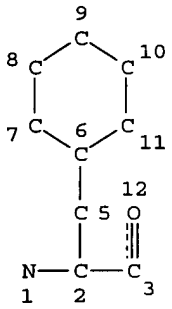
```
=> b reg
FILE 'REGISTRY' ENTERED AT 13:44:37 ON 13 JAN 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   12 JAN 2006  HIGHEST RN 871870-74-5
DICTIONARY FILE UPDATES:  12 JAN 2006  HIGHEST RN 871870-74-5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005.  A new display format, IDERL, is now    *
* available and contains the CA role and document type information. *
*                                                                    *
**********************************************************************

Structure search iteration limits have been increased.  See HELP SLIMITS
for details.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=> d que sta l12
L11             STR
```




```
NODE ATTRIBUTES:
CONNECT IS E2  RC AT   1
CONNECT IS E3  RC AT   3
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  10

STEREO ATTRIBUTES: NONE
L12         5852 SEA FILE=REGISTRY CSS FUL L11
```

100.0% PROCESSED 46604 ITERATIONS 5852 ANSWERS
SEARCH TIME: 00.00.01

=> d que sta l20
L18 STR



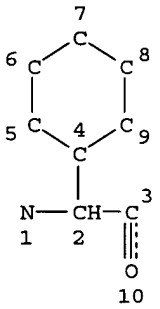
NODE ATTRIBUTES:
CONNECT IS E2 RC AT 1
CONNECT IS E3 RC AT 3
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 11

STEREO ATTRIBUTES: NONE
L20 9238 SEA FILE=REGISTRY CSS FUL L18

100.0% PROCESSED 60539 ITERATIONS 9238 ANSWERS
SEARCH TIME: 00.00.01

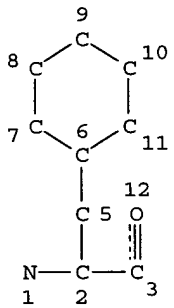
=> d que sta l21
L11 STR



NODE ATTRIBUTES:
CONNECT IS E2 RC AT 1
CONNECT IS E3 RC AT 3
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 10

STEREO ATTRIBUTES: NONE
L12 5852 SEA FILE=REGISTRY CSS FUL L11
L16 235539 SEA FILE=REGISTRY ABB=ON PLU=ON ([VALI'NLE'NQSTYRK'ORN'][VALI 'NLE'STYP'CIT'RK'ORN'HEDW'CHA']'CHA'[P'AZE'][YF][RK'ORN''HAR']) |([VALI'NLE'NQSTYRK'ORN'].{2}[P'AZE'][YF][RK'ORN''HAR'])/SQSP
L18 STR



NODE ATTRIBUTES:
CONNECT IS E2 RC AT 1
CONNECT IS E3 RC AT 3
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 11

STEREO ATTRIBUTES: NONE
L20 9238 SEA FILE=REGISTRY CSS FUL L18
L21 18 SEA FILE=REGISTRY ABB=ON PLU=ON (L12 OR L20) AND L16

=> b hcap
FILE 'HCAPLUS' ENTERED AT 13:44:54 ON 13 JAN 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 13 Jan 2006 VOL 144 ISS 4
FILE LAST UPDATED: 12 Jan 2006 (20060112/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d bib abs hitstr l26 tot

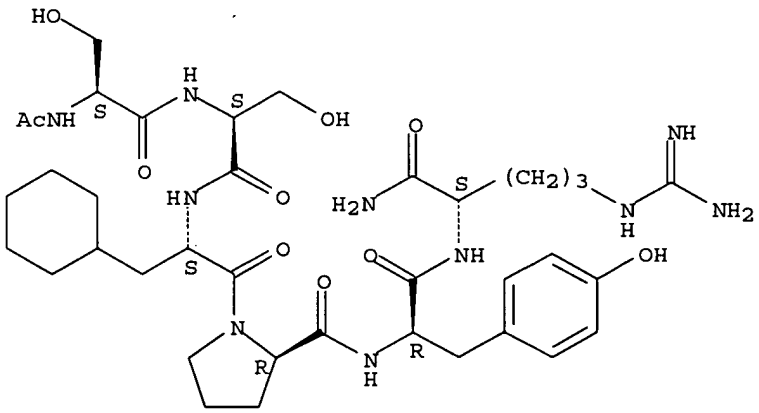
L26 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:605408 HCAPLUS
DN 141:134085
TI Peptidic compound thrombin inhibitors, and their diagnostic and

therapeutic use
IN **Thurk, Marcel**; Schwienhorst, Andreas
PA CPI Creative Pharma International GmbH, Germany
SO Ger. Offen., 13 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE--10301255	A1	20040729	2003DE-1001255	20030115
CA---2513466	AA	20040729	2004CA-2513466	20040115
WO2004063212	A2	20040729	2004WO-EP00256	20040115
WO2004063212	A3	20050324		
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GH, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA				
EP---1583587	A2	20051012	2004EP-0702312	20040115
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRAI 2003DE-1001255	A	20030115		
2004WO-EP00256	W	20040115		

OS MARPAT 141:134085
AB The invention discloses biol. active peptide compds. (Markush included) which interact with thrombin and inhibit it.
IT **501937-44-6 501937-44-6D**, salts **501937-46-8 501937-46-8D**, salts **501937-48-0 501937-48-0D**, salts **501937-49-1 501937-49-1D**, salts **501937-51-5 501937-51-5D**, salts **501937-55-9 501937-55-9D**, salts **501937-57-1 501937-57-1D**, salts **501937-60-6 501937-60-6D**, salts **501937-62-8 501937-62-8D**, salts
RL: DGN (Diagnostic use); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptidic compound thrombin inhibitors, and diagnostic and therapeutic use)
RN 501937-44-6 HCAPLUS
CN L-Argininamide, N-acetyl-L-seryl-L-seryl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

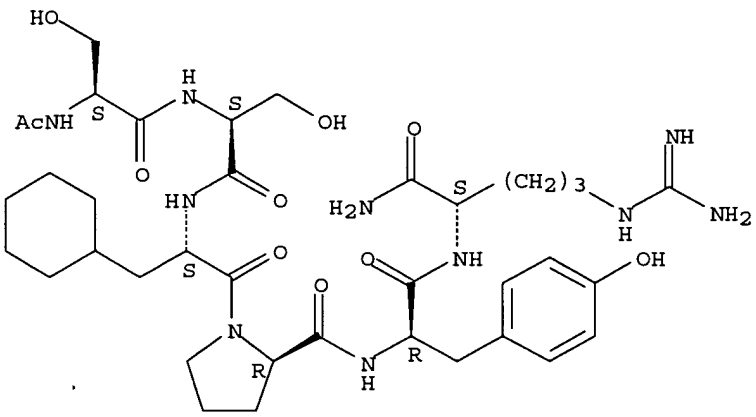
Absolute stereochemistry.



RN 501937-44-6 HCAPLUS
CN L-Argininamide, N-acetyl-L-seryl-L-seryl-3-cyclohexyl-L-alanyl-D-prolyl-D-

tyrosyl- (9CI) (CA INDEX NAME)

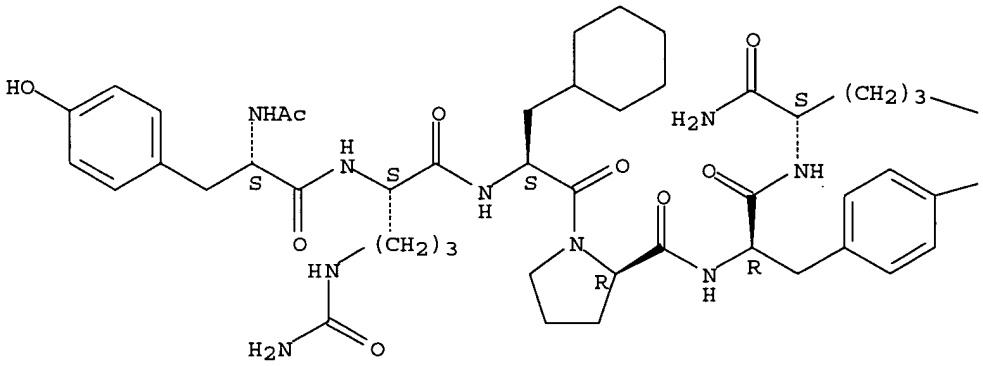
Absolute stereochemistry.



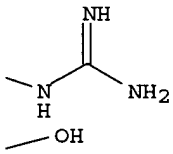
RN 501937-46-8 HCAPLUS
CN L-Argininamide, N-acetyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



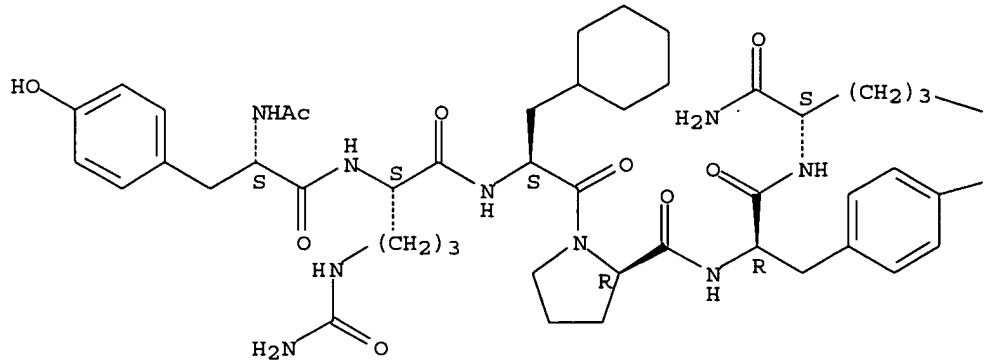
PAGE 1-B



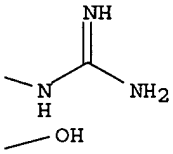
RN 501937-46-8 HCAPLUS
CN L-Argininamide, N-acetyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

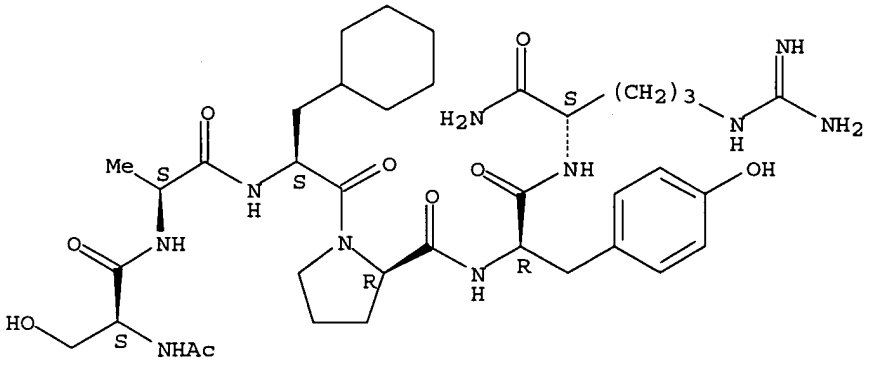


PAGE 1-B



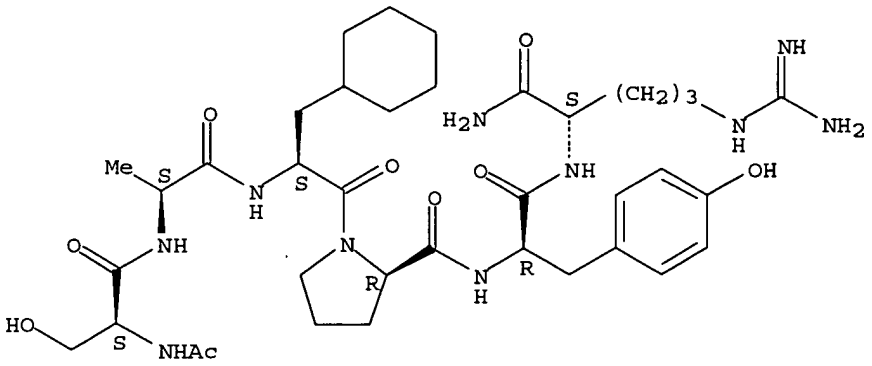
RN 501937-48-0 HCAPLUS
CN L-Argininamide, N-acetyl-L-seryl-L-alanyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 501937-48-0 HCAPLUS
CN L-Argininamide, N-acetyl-L-seryl-L-alanyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

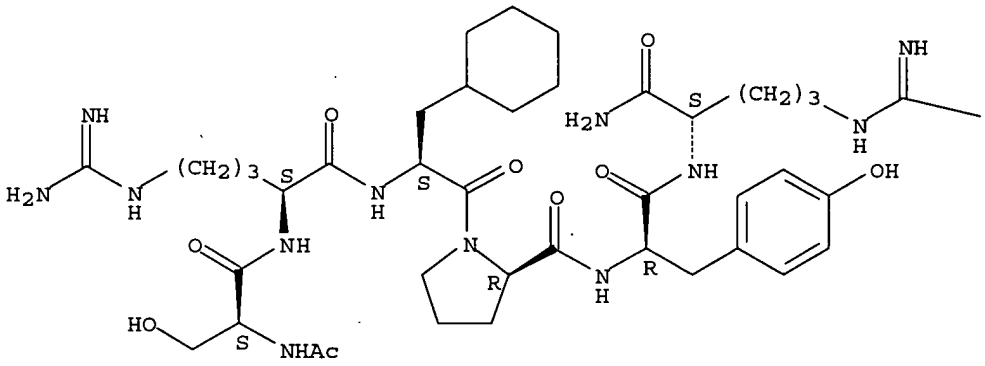
Absolute stereochemistry.



RN 501937-49-1 HCAPLUS
CN L-Argininamide, N-acetyl-L-seryl-L-arginyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



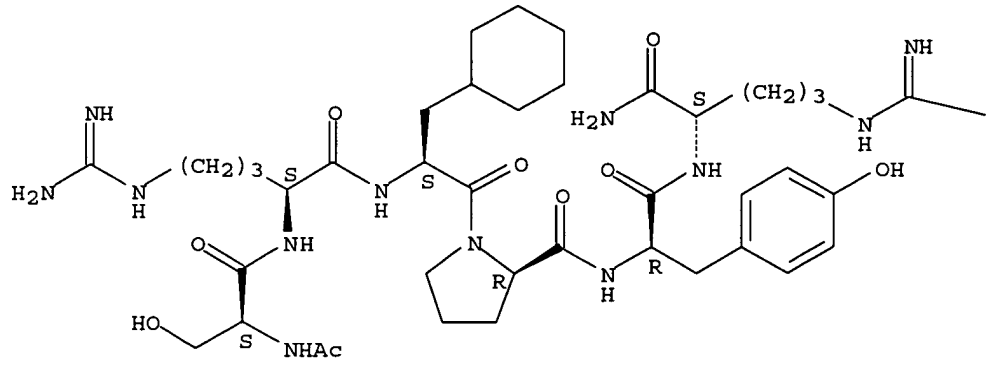
PAGE 1-B

—NH2

RN 501937-49-1 HCAPLUS
CN L-Argininamide, N-acetyl-L-seryl-L-arginyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

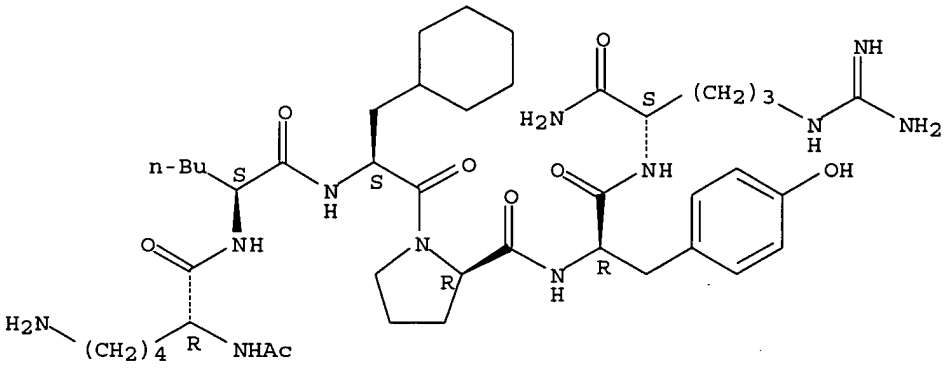


PAGE 1-B

NH_2

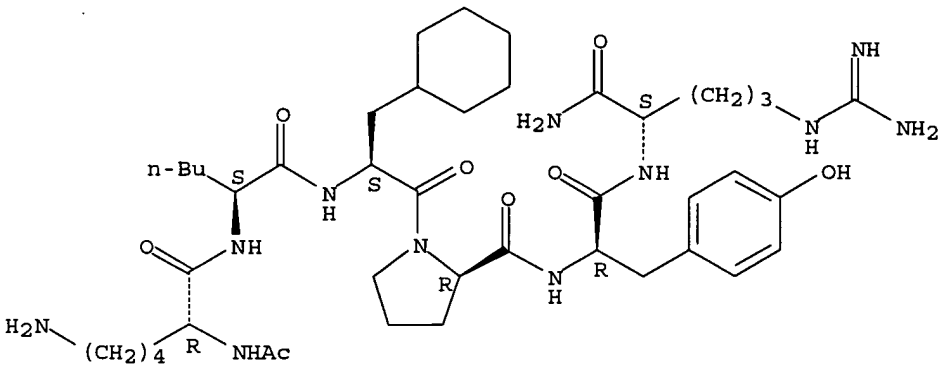
RN 501937-51-5 HCAPLUS
CN L-Argininamide, N2-acetyl-D-lysyl-L-norleucyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



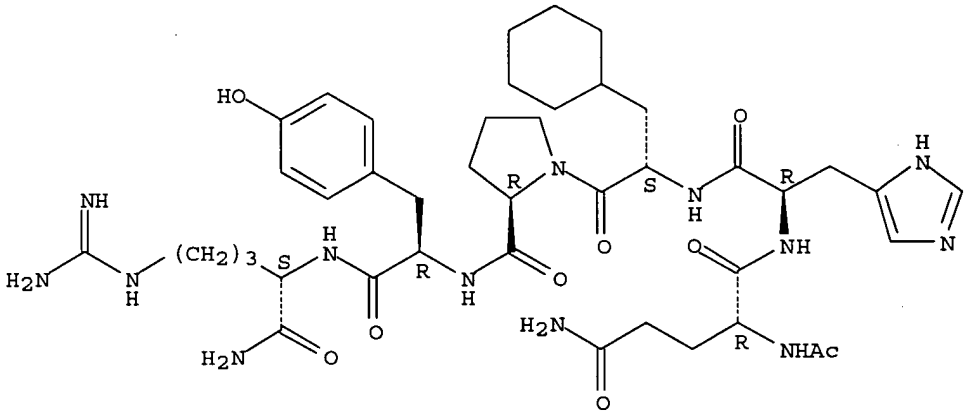
RN 501937-51-5 HCAPLUS
CN L-Argininamide, N2-acetyl-D-lysyl-L-norleucyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



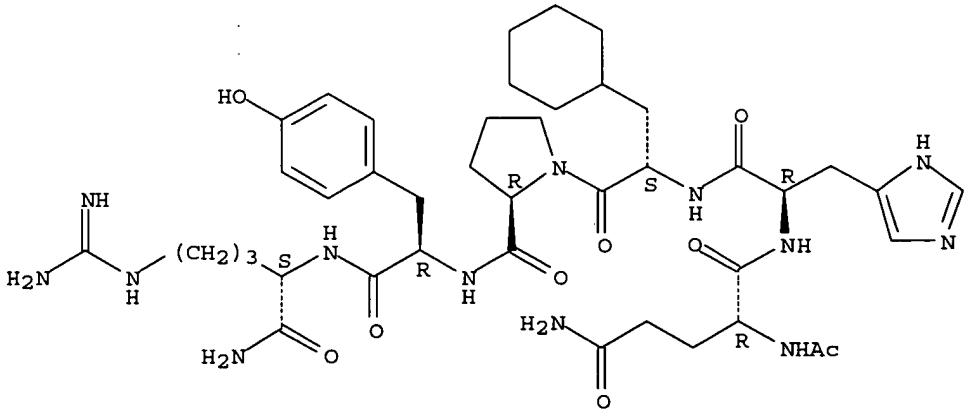
RN 501937-55-9 HCAPLUS
CN L-Argininamide, N2-acetyl-D-glutaminyl-D-histidyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 501937-55-9 HCAPLUS
CN L-Argininamide, N2-acetyl-D-glutaminyl-D-histidyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

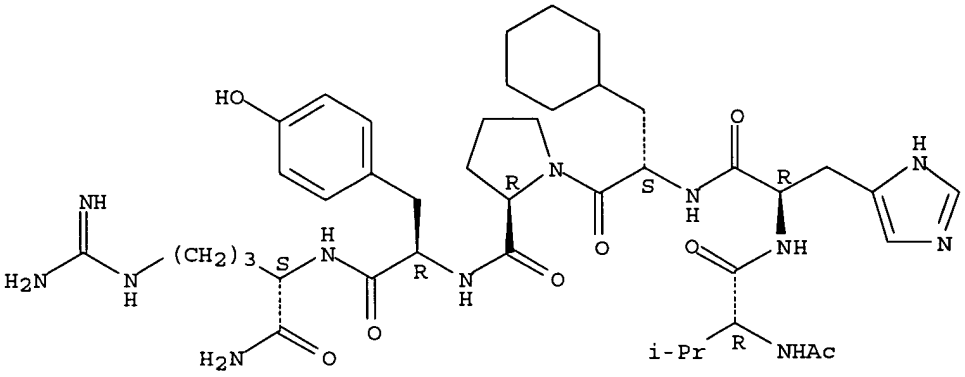
Absolute stereochemistry.



RN 501937-57-1 HCAPLUS

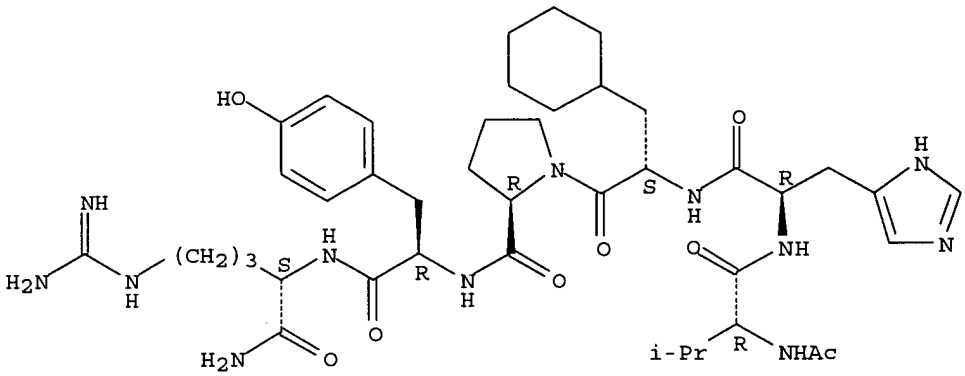
CN L-Argininamide, N-acetyl-D-valyl-D-histidyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 501937-57-1 HCAPLUS
CN L-Argininamide, N-acetyl-D-valyl-D-histidyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

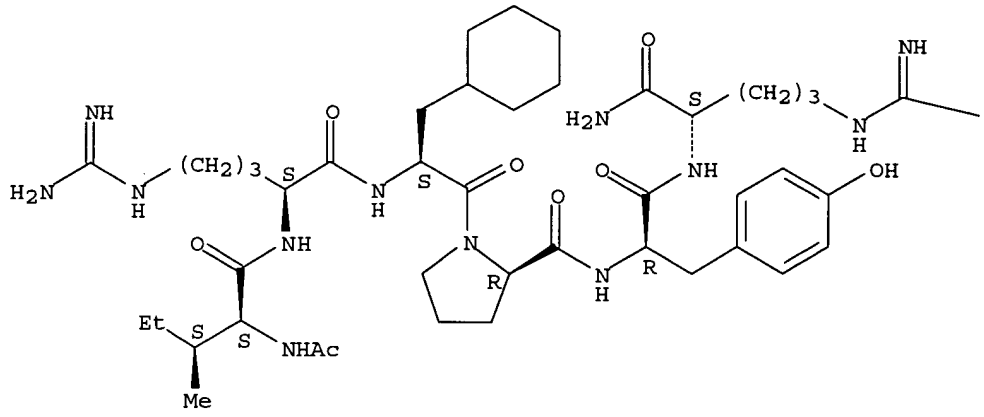
Absolute stereochemistry.



RN 501937-60-6 HCAPLUS
CN L-Argininamide, N-acetyl-L-isoleucyl-L-arginyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



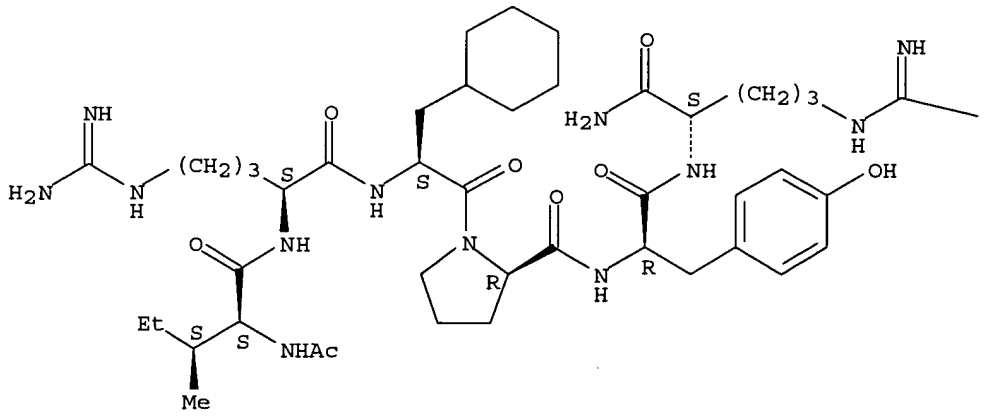
PAGE 1-B

—NH_2

RN 501937-60-6 HCAPLUS
CN L-Argininamide, N-acetyl-L-isoleucyl-L-arginyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

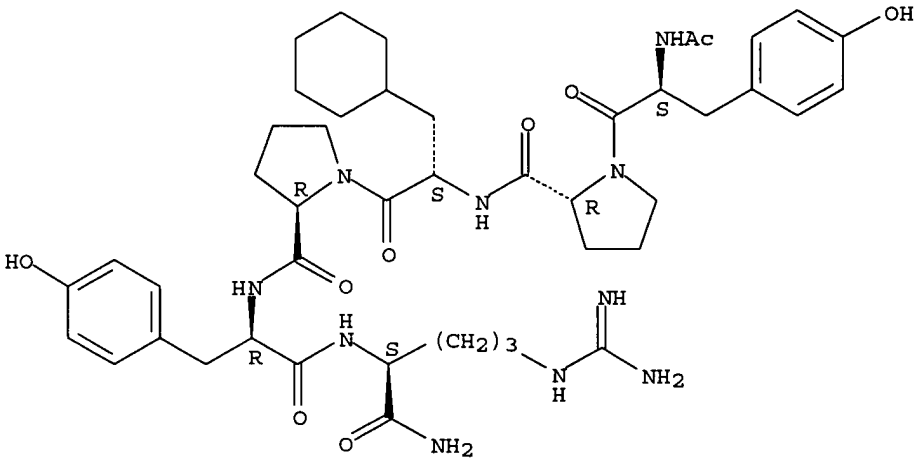


PAGE 1-B

—NH_2

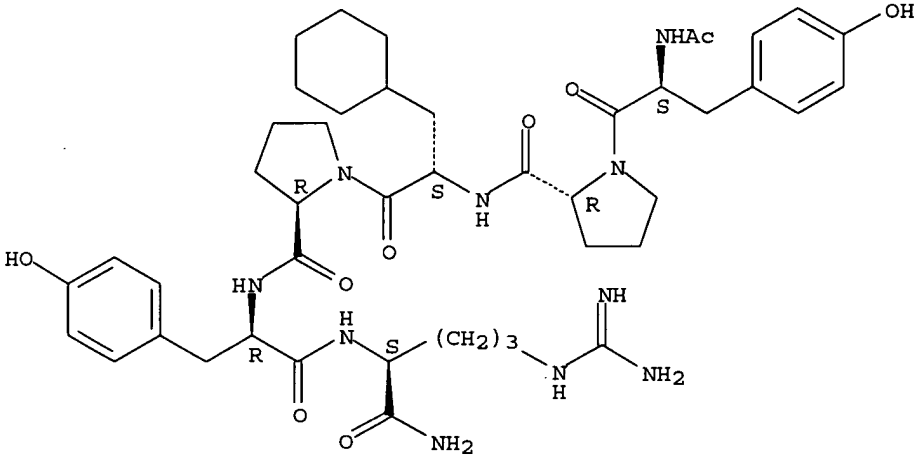
RN 501937-62-8 HCAPLUS
CN L-Argininamide, N-acetyl-L-tyrosyl-D-prolyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 501937-62-8 HCAPLUS
CN L-Argininamide, N-acetyl-L-tyrosyl-D-prolyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L26 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:221711 HCAPLUS
DN 138:238448
TI Synthesis of peptides for use as thrombin inhibitors for therapeutic use
IN **Thurk, Marcel**
PA **Novel Science** International Gmbh, Germany
SO PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI	WO2003022873	A1	20030320	2002WO-EP10137	20020910 <--
	WO2003022873	C2	20031211		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	DE--10146632	A1	20050203	2001DE-1046632	20010921 <--
	DE--10156995	A1	20050210	2001DE-1056995	20011121 <--
	DE--10200666	A1	20050630	2002DE-1000666	20020110 <--
	CA---2460300	AA	20030320	2002CA-2460300	20020910 <--
	EP---1425296	A1	20040609	2002EP-0797977	20020910 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
	US2005026843	A1	20050203	2004US-0798218	20040310 <--
PRAI	2001DE-1044340	A	20010910 <--		
	2001DE-1046632	A	20010921 <--		
	2001DE-1049678	A	20011009 <--		
	2001DE-1056995	A	20011121 <--		
	2002DE-1000666	A	20020110 <--		
	2002WO-EP10137	W	20020910 <--		

OS MARPAT 138:238448

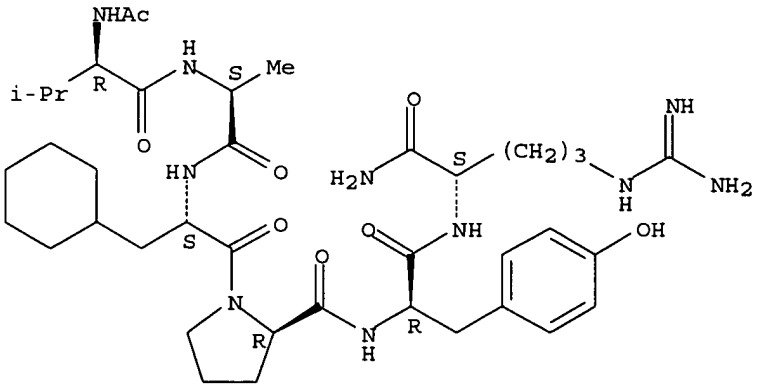
AB The invention relates to biol. active mols., interacting with thrombin and inhibiting the same. The invention particularly relates to mols. of general formula Y-(NH-X-C=O)-(NH-X1-C=O)-(NH-X2-C=O)-(NH-X3-C=O)-(NH-X4-C=O)(NH-X5-C=O)-Y1, [Y,Y1 = protecting groups; X, X1-5 = D- or L-natural or synthetic amino acids] or N-or C-terminal shortened variants of said compds. and the use thereof for the production of medicaments (no data). Thus, solid-phase peptide synthesis was used to prepare H3CC(O)-L-Arg-L-Cha-D-Pro-D-Tyr-L-Arg-NH2 (Cha = cyclohexylalanine) (I) (no data). In in vitro thrombin inhibition testing, I had an anti-amidase activity of 98% at 10μM.

IT **501937-40-2P 501937-41-3P 501937-44-6P**
501937-45-7P 501937-46-8P 501937-47-9P
501937-48-0P 501937-49-1P 501937-50-4P
501937-51-5P 501937-53-7P 501937-55-9P
501937-57-1P 501937-60-6P 501937-62-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptides for use as thrombin inhibitors for therapeutic use)

RN 501937-40-2 HCAPLUS

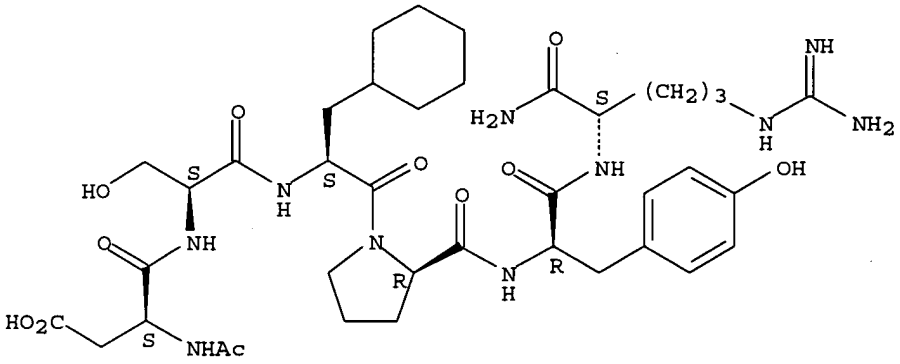
CN L-Argininamide, N-acetyl-D-valyl-L-alanyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



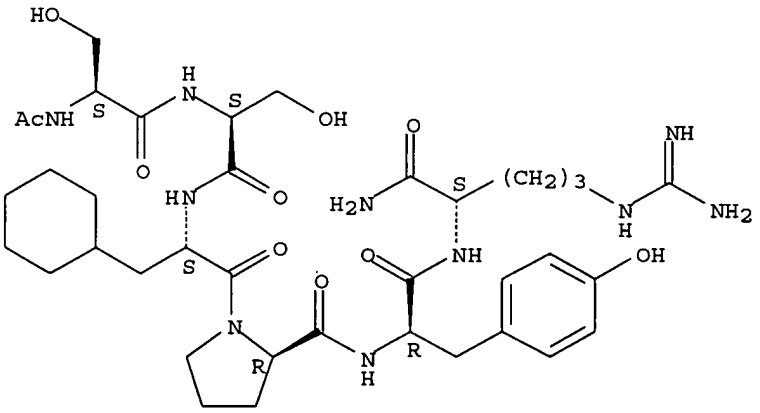
RN 501937-41-3 HCAPLUS
CN L-Argininamide, N-acetyl-L-α-aspartyl-L-seryl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 501937-44-6 HCAPLUS
CN L-Argininamide, N-acetyl-L-seryl-L-seryl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

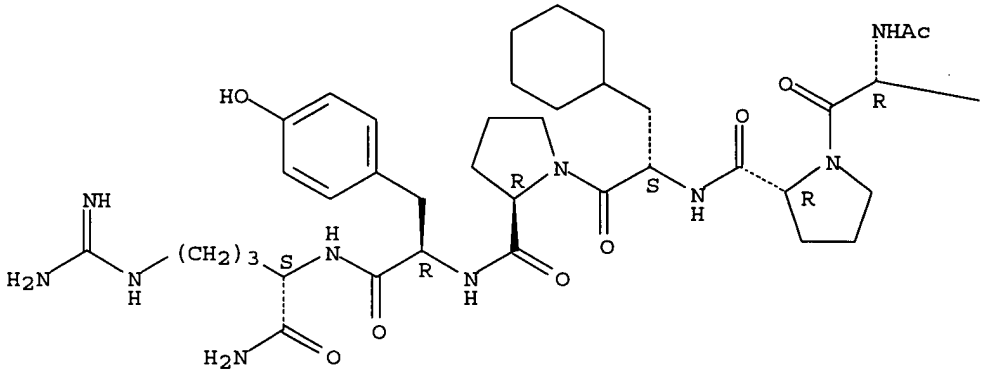


RN 501937-45-7 HCAPLUS
CN L-Argininamide, N2-acetyl-D-lysyl-D-prolyl-3-cyclohexyl-L-alanyl-D-prolyl-

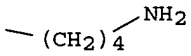
D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



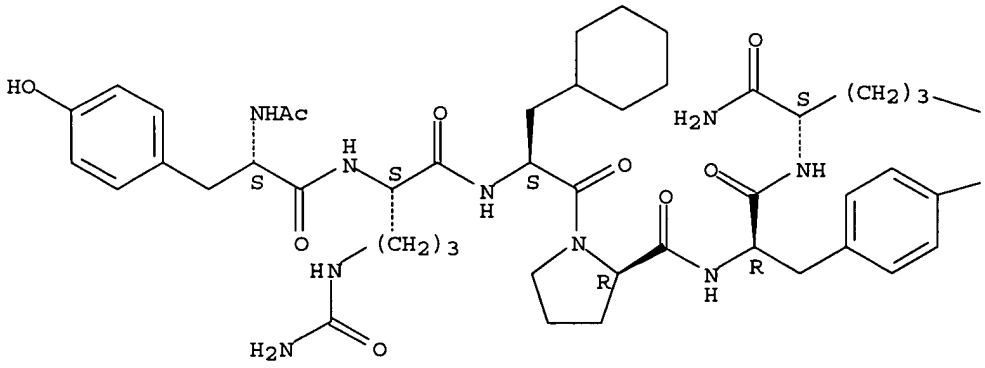
PAGE 1-B



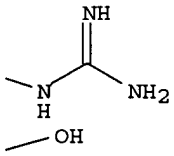
RN 501937-46-8 HCAPLUS
CN L-Argininamide, N-acetyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

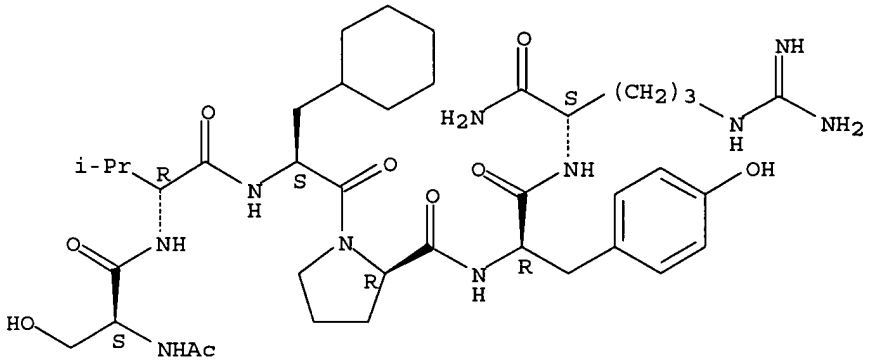


PAGE 1-B



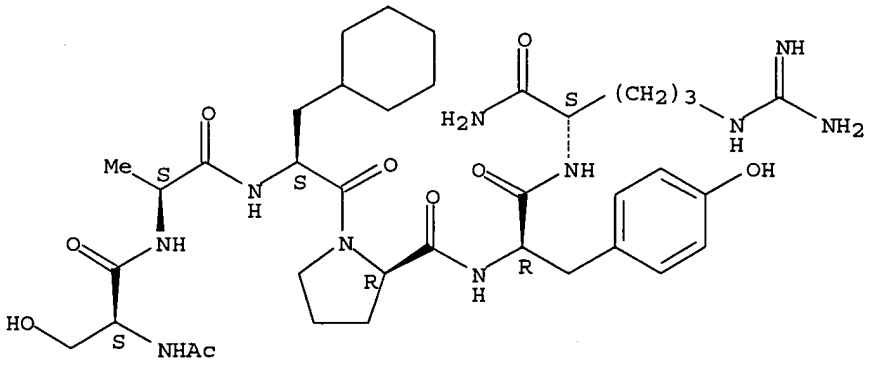
RN 501937-47-9 HCAPLUS
CN L-Argininamide, N-acetyl-L-seryl-D-valyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 501937-48-0 HCAPLUS
CN L-Argininamide, N-acetyl-L-seryl-L-alanyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

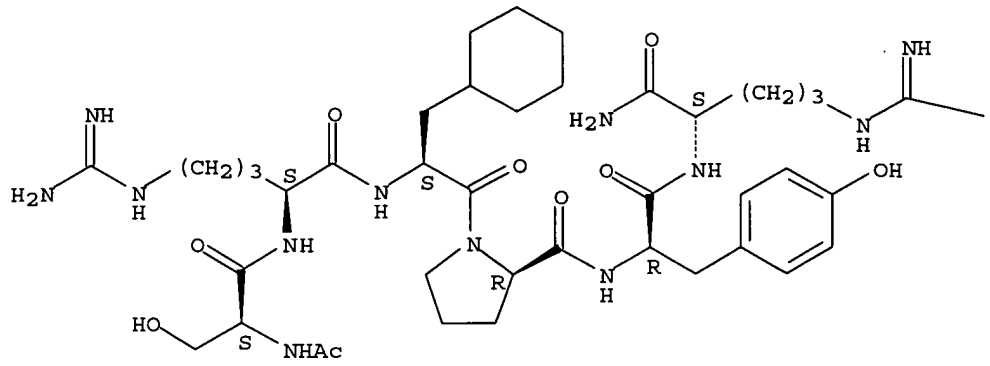
Absolute stereochemistry.



RN 501937-49-1 HCAPLUS
CN L-Argininamide, N-acetyl-L-seryl-L-arginyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

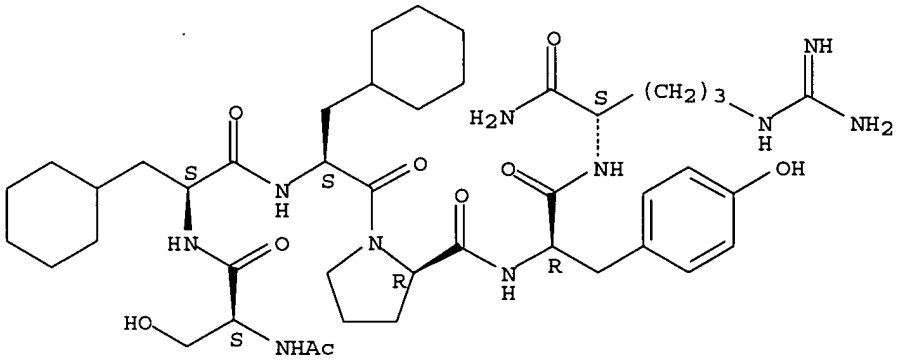
PAGE 1-A



PAGE 1-B

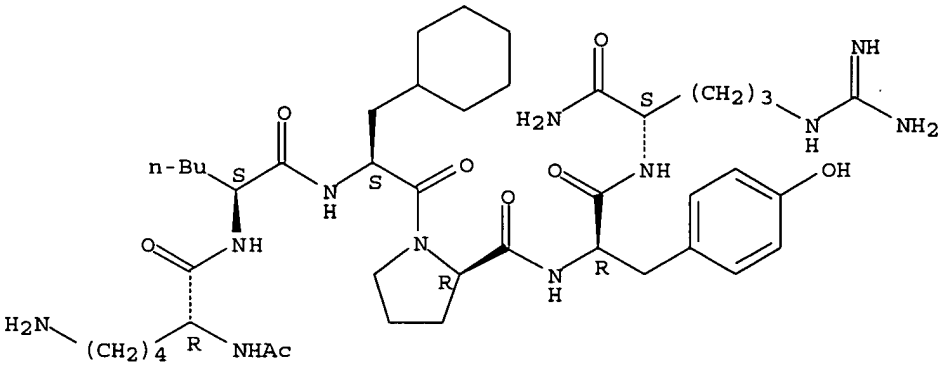
RN 501937-50-4 HCAPLUS
CN L-Argininamide, N-acetyl-L-seryl-3-cyclohexyl-L-alanyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



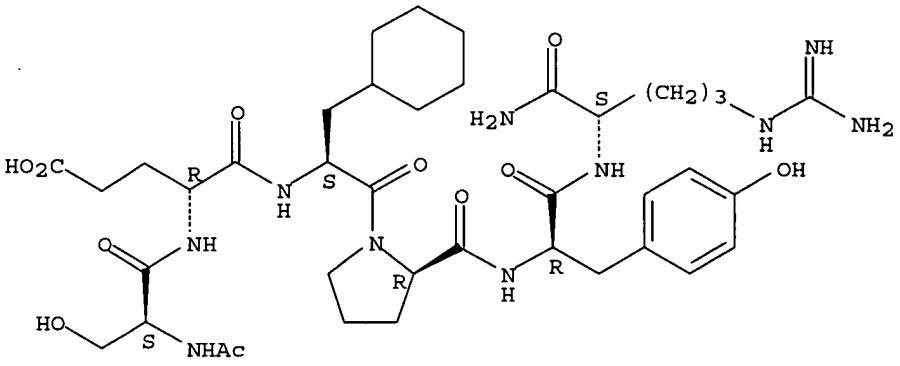
RN 501937-51-5 HCAPLUS
CN L-Argininamide, N2-acetyl-D-lysyl-L-norleucyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



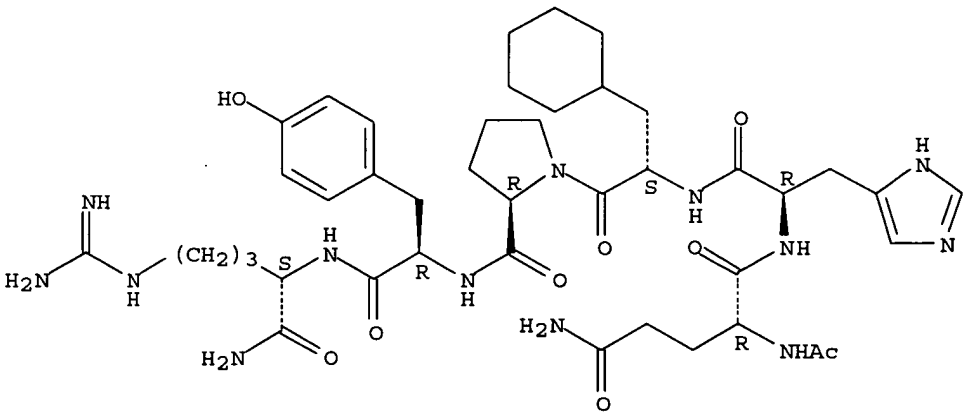
RN 501937-53-7 HCAPLUS
CN L-Argininamide, N-acetyl-L-seryl-D-α-glutamyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



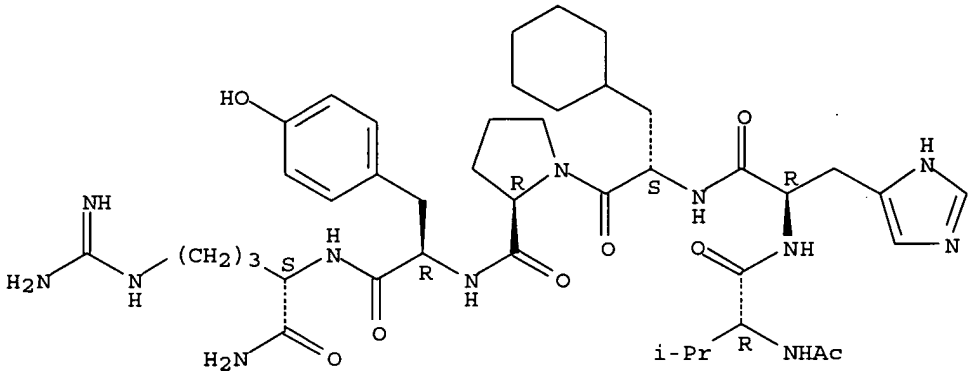
RN 501937-55-9 HCAPLUS
CN L-Argininamide, N2-acetyl-D-glutaminyl-D-histidyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 501937-57-1 HCAPLUS
CN L-Argininamide, N-acetyl-D-valyl-D-histidyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

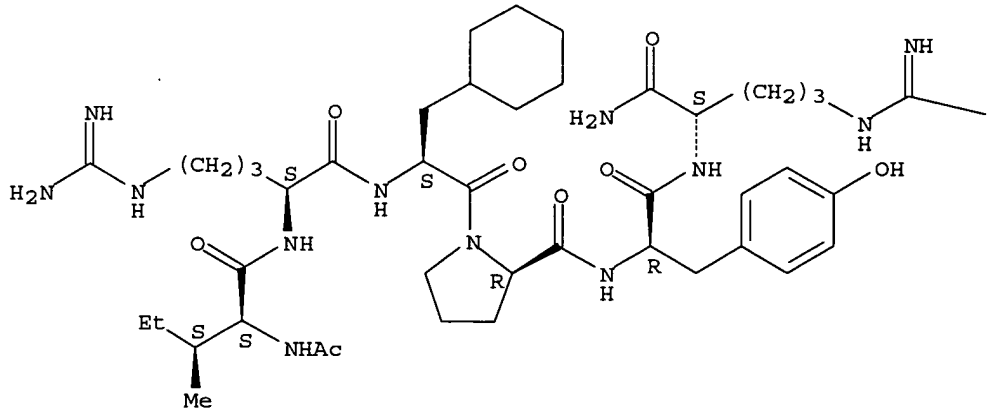
Absolute stereochemistry.



RN 501937-60-6 HCAPLUS
CN L-Argininamide, N-acetyl-L-isoleucyl-L-arginyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

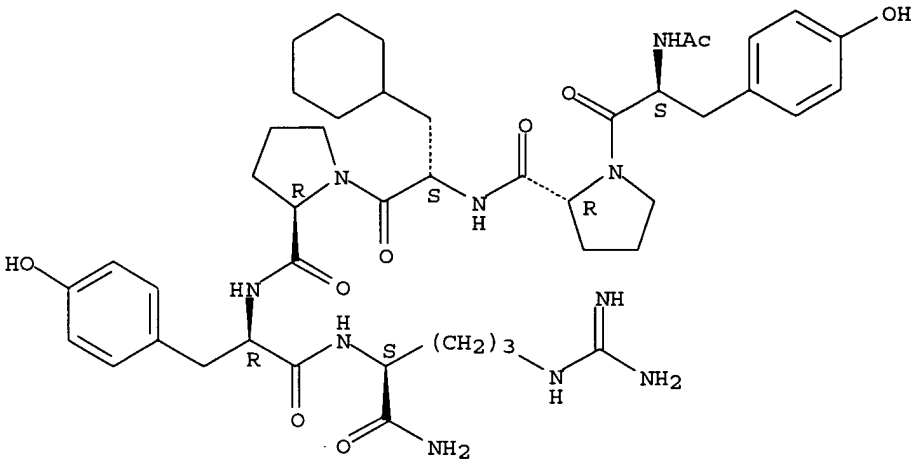
PAGE 1-A



PAGE 1-B

RN 501937-62-8 HCAPLUS
CN L-Argininamide, N-acetyl-L-tyrosyl-D-prolyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



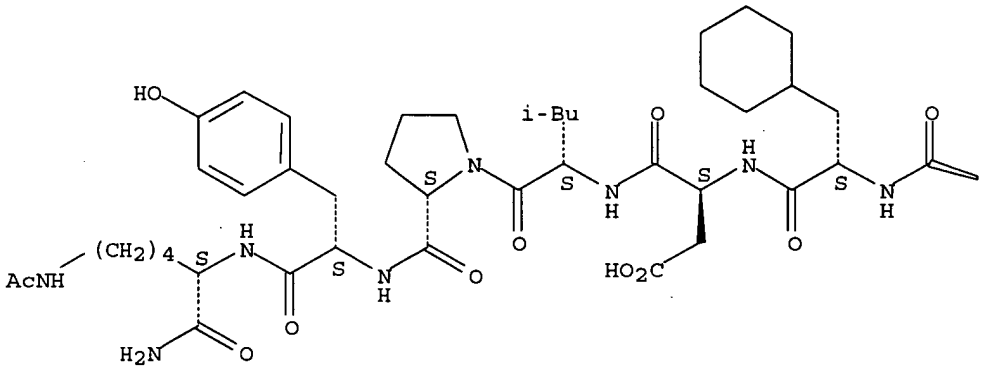
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:675049 HCAPLUS
DN 134:27426
TI Optimization of the P'-Region of Peptide Inhibitors of Hepatitis C Virus NS3/4A Protease
AU Ingallinella, Paolo; Bianchi, Elisabetta; Ingenito, Raffaele; Koch, Uwe; Steinkuehler, Christian; Altamura, Sergio; Pessi, Antonello
CS IRBM P. Angeletti, Pomeza, 00040, Italy
SO Biochemistry (2000), 39(42), 12898-12906
CODEN: BICHAW; ISSN: 0006-2960
PB American Chemical Society
DT Journal
LA English
AB Infection by Hepatitis C Virus (HCV) leads to a slowly progressing disease that over two decades can lead to liver cirrhosis or liver cancer. Currently, one of the most promising approaches to anti-HCV therapy is the development of inhibitors of the NS3/4A protease, which is essential for maturation of the viral polyprotein. Several substrate-derived inhibitors of NS3/4A have been described, all taking advantage of binding to the S subsite of the enzyme. Inspection of the S' subsite of NS3/4A shows binding pockets which might be exploited for inhibitor binding, but due to the fact that ground-state binding to the S' subsite is not used by the substrate, this does not represent a suitable starting point. The authors have now optimized S'-binding in the context of noncleavable decapeptides spanning P6-P4'. Binding was sequentially increased by introduction of the previously optimized P-region [Ingallinella et al. (1998) Biochem. 37, 8906-8914], change of the P4' residue, and combinatorial optimization of positions P2'-P3'. The overall process led to an increase in binding of more than 3 orders of magnitude, with the best decapeptide showing IC50 < 200 pM. The binding mode of the decapeptides described in the present work shares features with the binding mode of the natural substrates, together with novel interactions within the S' subsite. Therefore, these peptides may represent an entry point for a novel class of NS3 inhibitors.
IT **311348-38-6**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(optimization of P'-region of peptide inhibitors of hepatitis C virus NS3/4A protease in relation to antiviral therapy)
RN 311348-38-6 HCAPLUS
CN L-Lysinamide, N-acetyl-L-α-aspartyl-D-α-glutamyl-L-leucyl-L-isoleucyl-3-cyclohexyl-L-alanyl-L-cysteinyl-L-prolyl-3-cyclohexyl-L-alanyl-

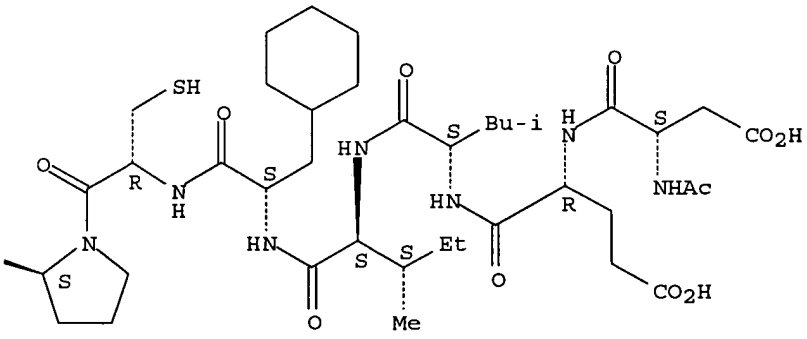
L-α-aspartyl-L-leucyl-L-prolyl-L-tyrosyl-N6-acetyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:368424 HCAPLUS
DN 133:12727
TI Peptidic pharmaceutical compounds for the inhibition of hepatitis C virus NS3 protease
IN Pessi, Antonello; Ingallinella, Paola; Bianchi, Elisabetta
PA Istituto di Ricerche di Biologia Molecolare p Angeletti Spa, Italy
SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO2000031129	A1	20000602	1999WO-EP09207	19991124

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,

IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA---2352493	AA	20000602	1999CA-2352493		19991124
EP---1144446	A1	20011017	1999EP-0972641		19991124
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
AU----764589	B2	20030821	2000AU-0013871		19991124
PRAI 1998GB-0025946	A	19981126			
1999WO-EP09207	W	19991124			

OS MARPAT 133:12727

AB Peptidic inhibitors of hepatitis C virus NS3 protease are disclosed which are based on the P and P' regions of the natural substrate. The P' part of the inhibitor is optimized to achieve maximum binding energy through interaction with the S' region of the enzyme. By selecting amino acids such that the inhibitor is substantially not cleavable by the NS3 protease, inhibitors having potency in the low nanomolar to sub-nanomolar range can be achieved.

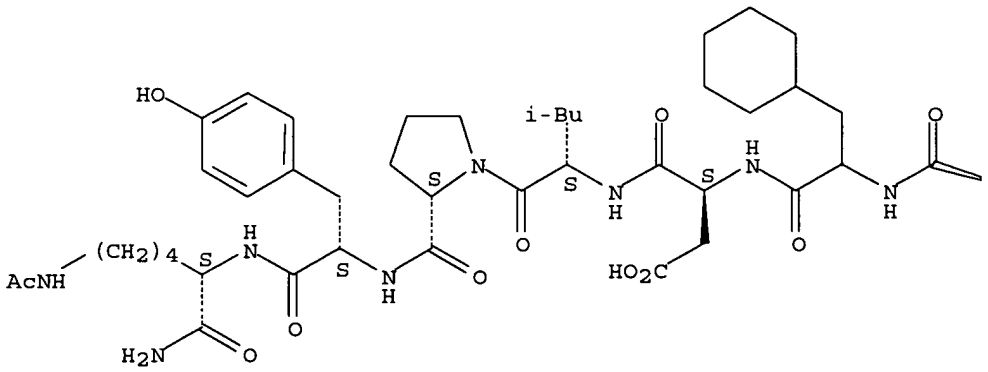
IT **272435-79-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(peptidic pharmaceutical compds. for inhibition of hepatitis C virus NS3 protease)

RN 272435-79-7 HCAPLUS

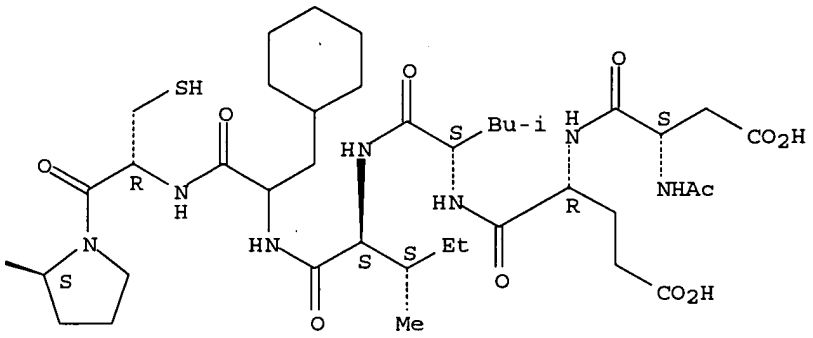
CN L-Lysinamide, N-acetyl-L-α-aspartyl-D-α-glutamyl-L-leucyl-L-isoleucyl-3-cyclohexylalanyl-L-cysteinyl-L-prolyl-3-cyclohexylalanyl-L-α-aspartyl-L-leucyl-L-prolyl-L-tyrosyl-N6-acetyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



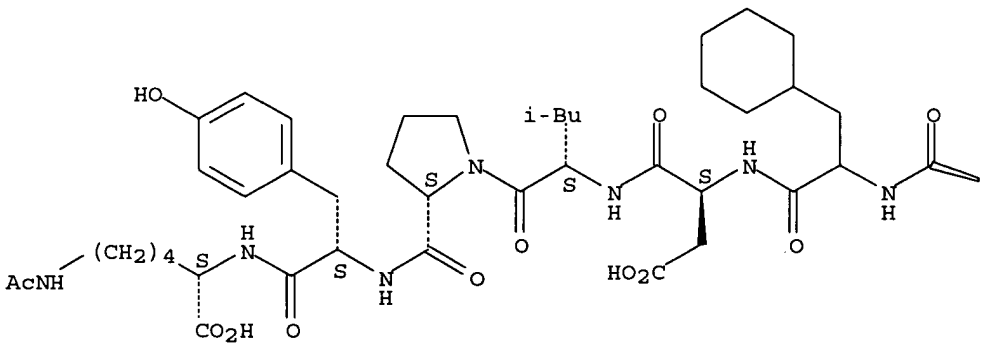
IT **272435-97-9 272784-99-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptidic pharmaceutical compds. for inhibition of hepatitis C virus NS3 protease)

RN 272435-97-9 HCAPLUS

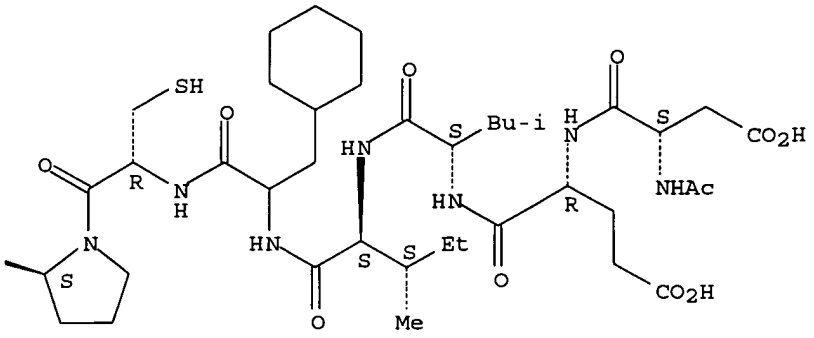
CN L-Lysine, N-acetyl-L-α-aspartyl-D-α-glutamyl-L-leucyl-L-isoleucyl-3-cyclohexylalanyl-L-cysteinyl-L-prolyl-3-cyclohexylalanyl-L-α-aspartyl-L-leucyl-L-prolyl-L-tyrosyl-N6-acetyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



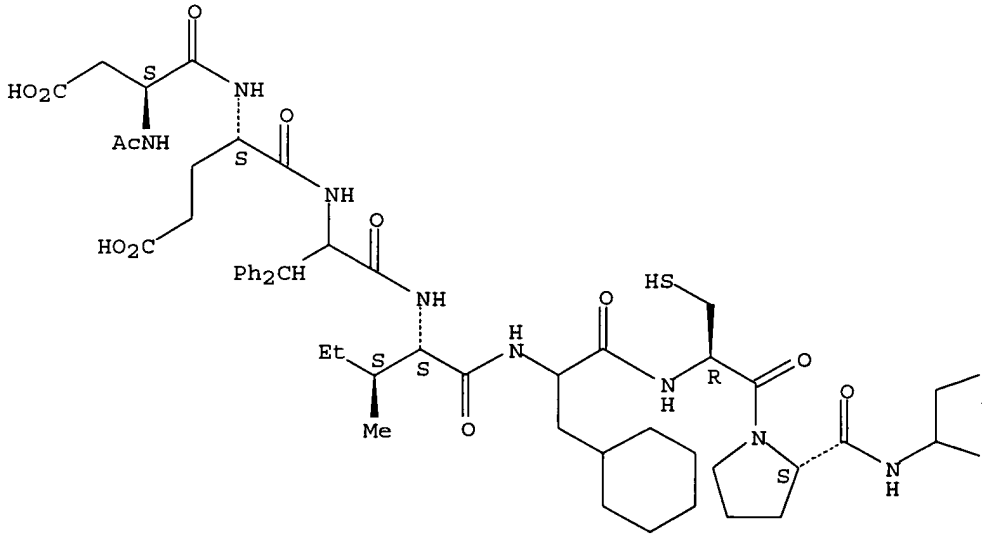
PAGE 1-B



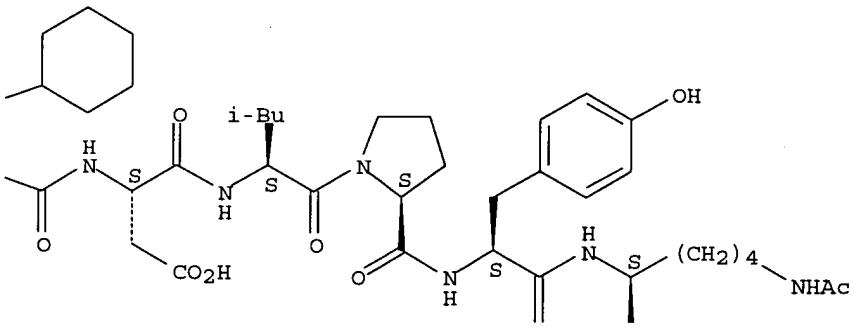
RN 272784-99-3 HCAPLUS
CN L-Lysine, N-acetyl-L-α-aspartyl-L-α-glutamyl-β-phenylphenylalanyl-L-isoleucyl-3-cyclohexylalanyl-L-cysteinyl-L-prolyl-3-cyclohexylalanyl-L-α-aspartyl-L-leucyl-L-prolyl-L-tyrosyl-N6-acetyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

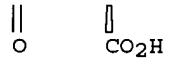
PAGE 1-A



PAGE 1-B



PAGE 2-B



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> b uspatall
FILE 'USPATFULL' ENTERED AT 13:45:25 ON 13 JAN 2006
CA INDEXING COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 13:45:25 ON 13 JAN 2006
CA INDEXING COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

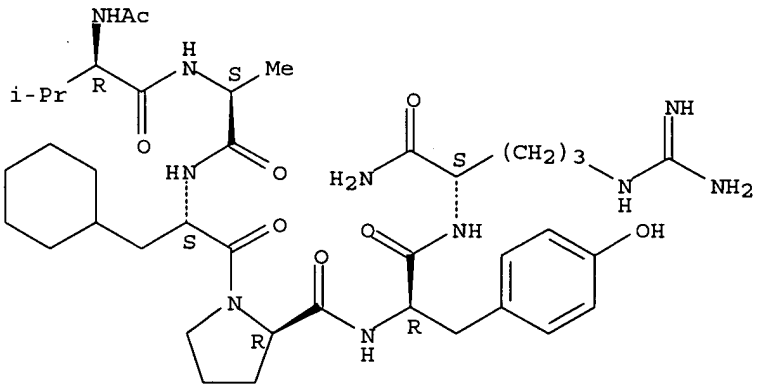
=> d bib abs hitstr l28

L28 ANSWER 1 OF 1 USPATFULL on STN
AN 2005:31406 USPATFULL
TI Organic compounds with biological activity as thrombin inhibitors and use thereof
IN Thurk, Marcel, Bovenden, GERMANY, FEDERAL REPUBLIC OF
PA Novel Science International GMBH, Gottingen, GERMANY, FEDERAL REPUBLIC OF (non-U.S. corporation)
PI US2005026843 A1 20050203
AI 2004US-0798218 A1 20040310 (10)
RLI Continuation of Ser. No. 2002WO-EP10137, filed on 10 Sep 2002, UNKNOWN
PRAI 2001DE-0144340 20010910
2001DE-0146632 20010921
2001DE-0149678 20011009
2001DE-0156995 20011121
DE 2002-10200666 20020110
DT Utility
FS APPLICATION
LREP DARBY & DARBY P.C., P. O. BOX 5257, NEW YORK, NY, 10150-5257

CLMN Number of Claims: 45
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1928
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to biologically active molecules, interacting with thrombin and inhibiting the same. The invention particularly relates to molecules of general formula (I):Y.sup.1--(NH--X.sup.1--C=0)--(NH--X.sup.2--C.dbd.C)--(NH--X.sup.3--C=0)--NH--X.sup.4--C=0)--(NH--X.sup.5--C=0)(NH--X.sup.6--C.dbd.0)--Y.sup.2, in which Y.sup.1, Y.sup.2, and X.sup.1-6 have the meanings given in the description, N.-or C-terminal shortened variants of said compounds and the use thereof for the production of medicaments.

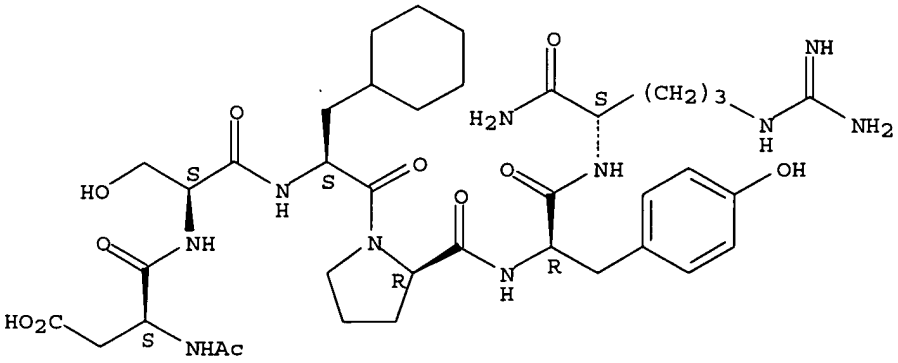
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **501937-40-2P 501937-41-3P 501937-44-6P**
501937-45-7P 501937-46-8P 501937-47-9P
501937-48-0P 501937-49-1P 501937-50-4P
501937-51-5P 501937-53-7P 501937-55-9P
501937-57-1P 501937-60-6P 501937-62-8P
(preparation of peptides for use as thrombin inhibitors for therapeutic use)
RN 501937-40-2 USPATFULL
CN L-Argininamide, N-acetyl-D-valyl-L-alanyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



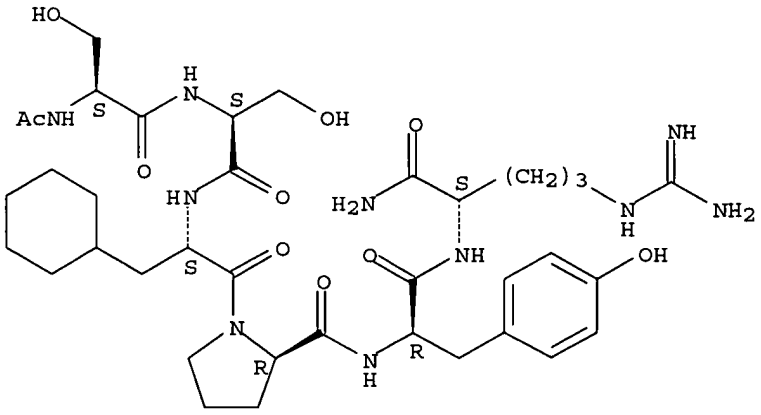
RN 501937-41-3 USPATFULL
CN L-Argininamide, N-acetyl-L-α-aspartyl-L-seryl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 501937-44-6 USPATFULL
CN L-Argininamide, N-acetyl-L-seryl-L-seryl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

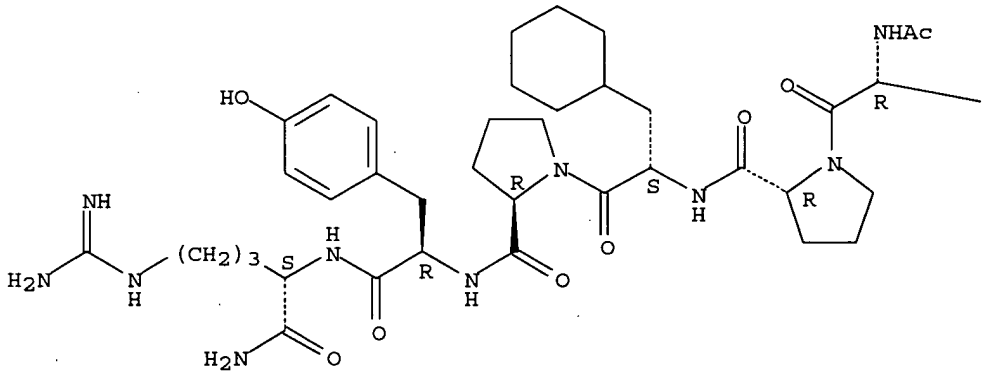
Absolute stereochemistry.



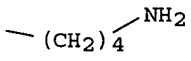
RN 501937-45-7 USPATFULL
CN L-Argininamide, N2-acetyl-D-lysyl-D-prolyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



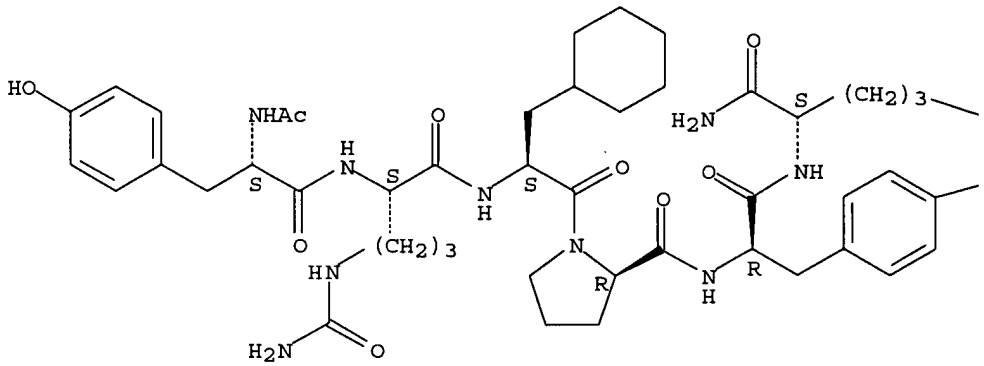
PAGE 1-B



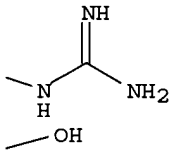
RN 501937-46-8 USPATFULL
CN L-Argininamide, N-acetyl-L-tyrosyl-N5-(aminocarbonyl)-L-ornithyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

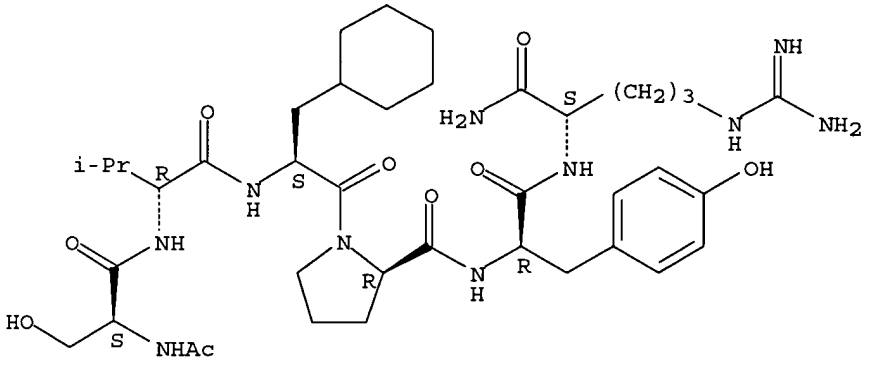


PAGE 1-B



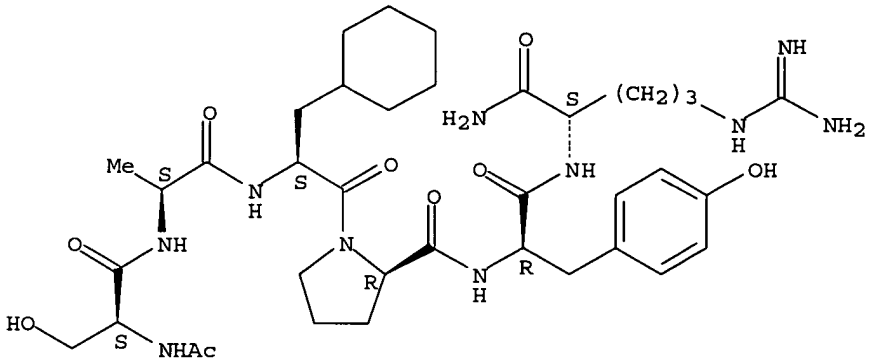
RN 501937-47-9 USPATFULL
CN L-Argininamide, N-acetyl-L-seryl-D-valyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 501937-48-0 USPATFULL
CN L-Argininamide, N-acetyl-L-seryl-L-alanyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

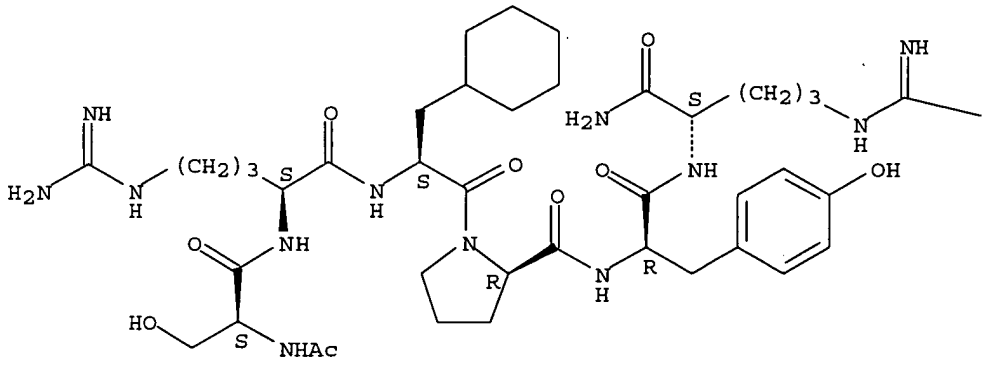
Absolute stereochemistry.



RN 501937-49-1 USPATFULL
CN L-Argininamide, N-acetyl-L-seryl-L-arginyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

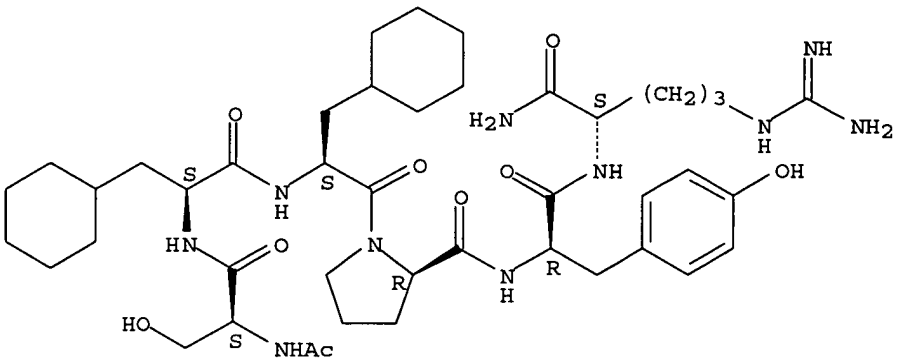
PAGE 1-A



PAGE 1-B

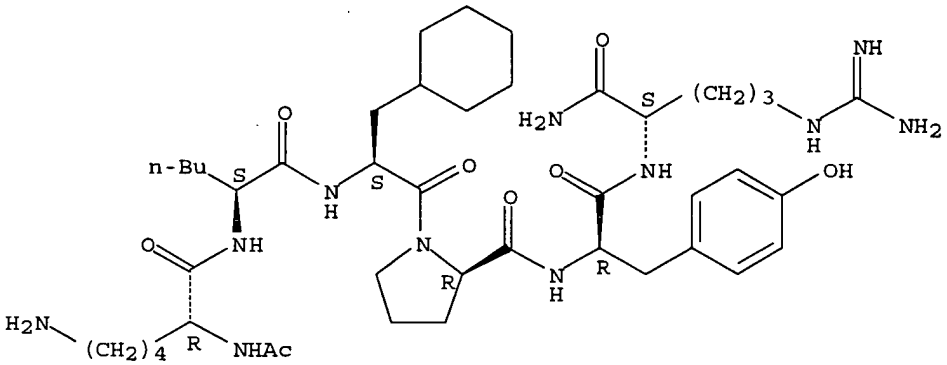
RN 501937-50-4 USPATFULL
CN L-Argininamide, N-acetyl-L-seryl-3-cyclohexyl-L-alanyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



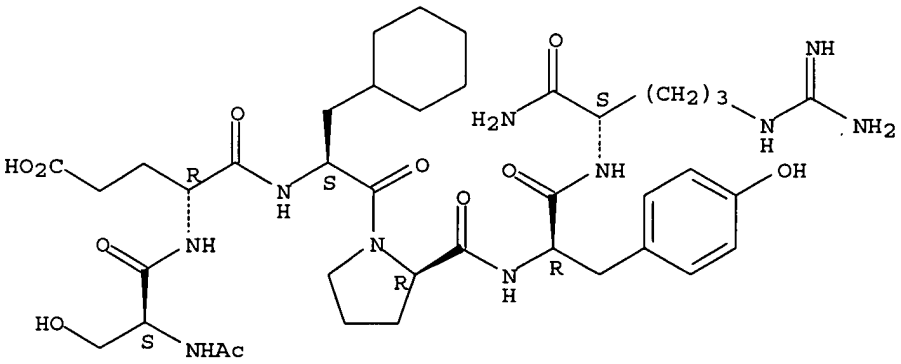
RN 501937-51-5 USPATFULL
CN L-Argininamide, N2-acetyl-D-lysyl-L-norleucyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



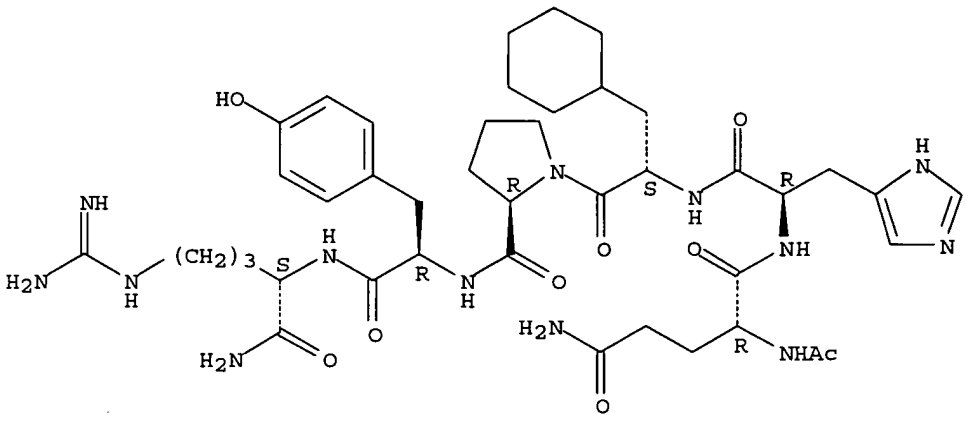
RN 501937-53-7 USPATFULL
CN L-Argininamide, N-acetyl-L-seryl-D-α-glutamyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



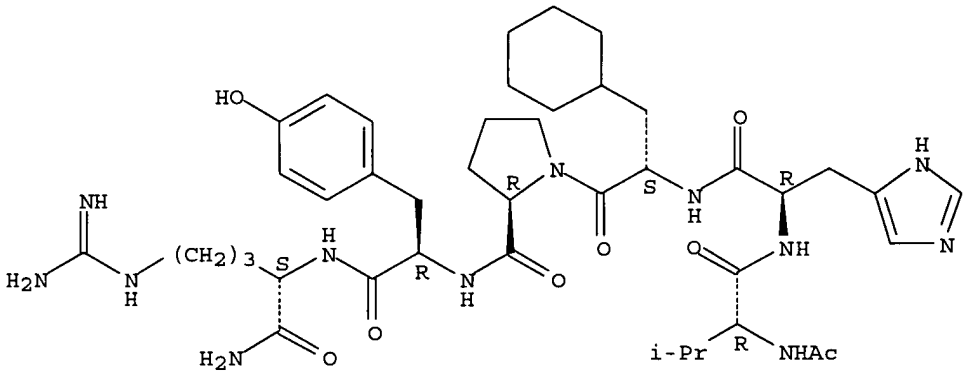
RN 501937-55-9 USPATFULL
CN L-Argininamide, N2-acetyl-D-glutaminyl-D-histidyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 501937-57-1 USPATFULL
CN L-Argininamide, N-acetyl-D-valyl-D-histidyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

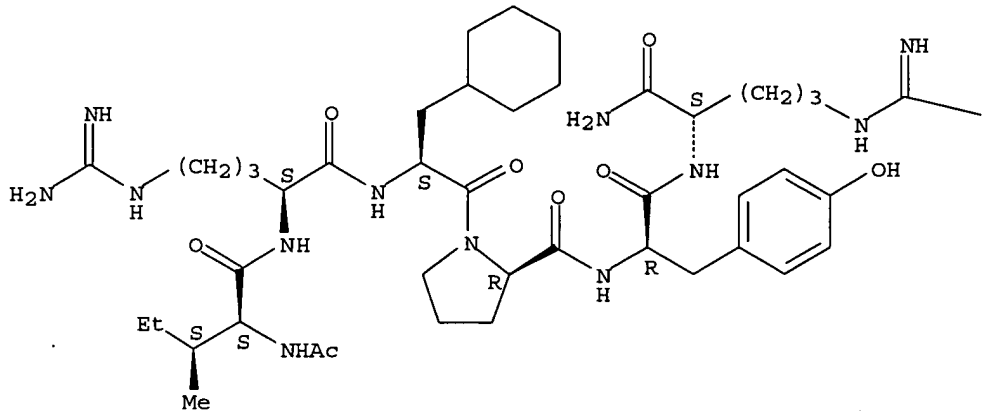
Absolute stereochemistry.



RN 501937-60-6 USPATFULL
CN L-Argininamide, N-acetyl-L-isoleucyl-L-arginyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

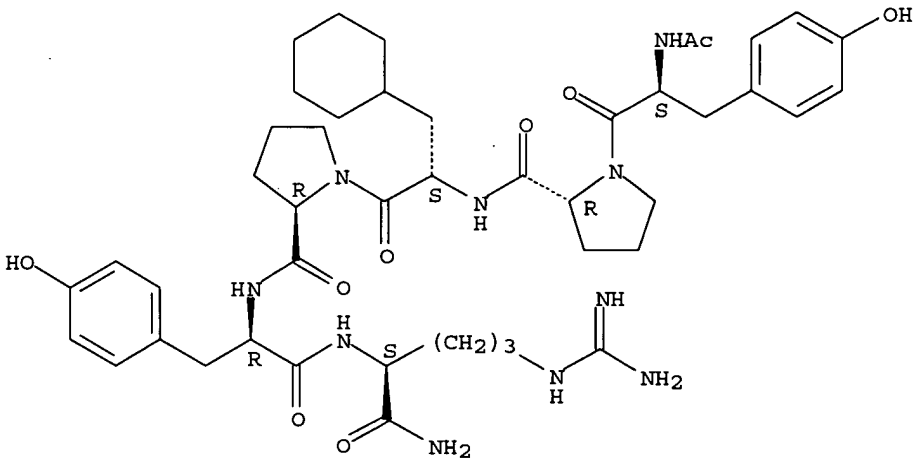


PAGE 1-B

—NH_2

RN 501937-62-8 USPATFULL
CN L-Argininamide, N-acetyl-L-tyrosyl-D-prolyl-3-cyclohexyl-L-alanyl-D-prolyl-D-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d his

(FILE 'HOME' ENTERED AT 12:28:39 ON 13 JAN 2006)

FILE 'HCAPLUS' ENTERED AT 12:28:59 ON 13 JAN 2006
L1 1 US2005026843/PN OR (US2004-798218# OR DE2002-10200666# OR DE200

```
     FILE 'REGISTRY' ENTERED AT 12:31:16 ON 13 JAN 2006

     FILE 'HCAPLUS' ENTERED AT 12:31:25 ON 13 JAN 2006
                E THURK M/AU
L2            10 E3-4
L3             5 (NOVEL (1W)SCIENCE)/CS,PA

     FILE 'REGISTRY' ENTERED AT 12:32:37 ON 13 JAN 2006

     FILE 'HCAPLUS' ENTERED AT 12:32:39 ON 13 JAN 2006
L4             TRA L1 1- RN :       44 TERMS

     FILE 'REGISTRY' ENTERED AT 12:32:40 ON 13 JAN 2006
L5            44 SEA L4
L6            43 L5 AND SQL/FA
L7               QUE [VALI'NLE'NQSTYRK'ORN'][VALI'NLE'STYP'CIT'RK'ORN'HEDW'CHA']
                 E CYCLOHEXYLGLYCINE/CN
L8            15 L6 AND SQL>=6

     FILE 'HCAPLUS' ENTERED AT 13:21:56 ON 13 JAN 2006
L9             2 L8
L10            2 L9 AND L1-3

     FILE 'REGISTRY' ENTERED AT 13:23:35 ON 13 JAN 2006
L11              STR
L12         5852 SEA FILE=REGISTRY CSS FUL L11
L13            0 L12 AND L5
L14          510 L12 AND 6-7/SQL
L15              QUE [VALI'NLE'NQSTYRK'ORN'].{2}[P'AZE'][YF][RK'ORN''HAR']/SQSP
L16       235539 L7|L15
                 E CYCLOHEXYLALANINE/CN
L17            1 E4
L18              STR
L19           50 L18 CSS
L20         9238 L18 CSS FULL
L21           18 L12,L20 AND L16
L22           14 L21 AND L5-6
L23            4 L21 NOT L22

     FILE 'HCAPLUS' ENTERED AT 13:42:26 ON 13 JAN 2006
L24            4 L21
L25            2 L24 AND L1-3
L26            4 L24,L25,L9-10

     FILE 'HCAOLD' ENTERED AT 13:43:44 ON 13 JAN 2006
L27            0 L21,L8

     FILE 'USPATFULL, USPAT2' ENTERED AT 13:44:01 ON 13 JAN 2006
L28            1 L21,L8

=>
```